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Editorial

Are All Joints Equal? Synovial Fluid Analysis in Periprosthetic Joint Infection

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Neutrophils play a key role when recruited into circulation and to sites of infection or inflammation. Synovial fluid Gram-staining and microbiological studies have been implemented for the diagnostic work-up of both native and prosthetic joint infections (PJIs) for many decades. Joint synovial fluid cell count and differential analysis has been traditionally used to elucidate the underlying cause of acute native arthritis. Leukocyte count and differential were introduced in the diagnostic workup of PJI between 1998 and 2004. Over the past 20 years, several studies assessed the diagnostic accuracy of leukocyte count and differential from synovial fluid in patients with suspected PJI [1-10]. These studies identified the optimal cut-off value for PJI diagnosis to be approximately more than one log lower than for native joint septic arthritis. In earlier studies, these lower values produced unit errors in the transition from native to prosthetic joints infection [11]. Leukocytes/μL or leukocytes/ $10^{-3}cm^3$ are the currently recommend units for synovial cell count analyses. In parallel to these studies, laboratory institutions switched from manual to automated cell counting [12, 13], and cell count cut-off values were extrapolated to arthroplasties other than hip and knee joints [14]. For simplicity, providers tend to use one single optimal cut-off value irrespective of anatomic location of the prosthetic joint.

Many preanalytical steps are required from joint aspiration to cell counting (see Table 1). Variability of these steps may influence the result. Various institutions use different machines for cell counting. Thus, it is conceivable that there are inter-institutional variations of the optimal cut-off cell count value for the diagnosis of PJI (Table 2). To the best of our knowledge, there are no published data assessing inter-machine or inter-institutional synovial fluid cell count comparisons in the diagnosis of PJI. In addition, many of studies on the optimal cut-off cell count for the diagnosis of PJI have included a mix of patients with acute, chronic, early or late infections. Therefore, from a clinical point of view, PJI should be suspected when falling above a range of cell count instead of a precise cut-off value (Table 2). In addition, synovial cell count result is only one of several diagnostic pieces that may lead to a definite diagnosis of PJI.

Cut-off values ranging from 2500 to 5000 leukocytes/μL and 60% to 89% for polymorphonuclear leukocytes (PMN) for the diagnosis of hip and knee PJI have been published [15]. The comparison of these studies is difficult because of the aforementioned variability of cell count results and lack of gold standard definition of PJI diagnosis. However, it seems that cut-off values for infection in total knee arthroplasty are lower than those in total hip arthroplasty (Table 2). The reason for this tendency is unclear but may be related to the anatomy, the size of the joint, synovial fluid volume and its vascularization. These arguments are in line with the observation that synovial fluid analysis is rarely possible in suspected ankle PJI [16].

In this issue of *JBJI*, Strahm and colleagues

investigated the optimal cut-off values in patients with shoulder PJI [17]. Their findings are compelling and surprising. Firstly, nearly a third of these cases (11 of 39 punctures) resulted in a dry tap. Secondly, the optimal cut-off value for PMN was in the rage of known values for the diagnosis of PJI (>54%). However, the cutoff for leukocyte count was 12,200/μL (sensitivity 100% and specificity 75%). Thirdly, infection due to low virulent organisms (e.g.; *Cutibacterium* spp.) were associated with a high synovial cell counts. The authors points towards the limitations of their study, including the small sample size and its retrospective nature. Consequently, the interpretation of these results require confirmation in a larger setting. Nonetheless, the work of Strahm et al. [17] may indicate that cutoffs value of cell count may be affected by joint site.

Table 1. Factors potentially influencing the results of cell count and differential result in synovial fluid.

Drugs in the joint (e.g.; local anaesthetics)
Insufficient puncture volume (≥ 1mL preferred)
Insufficient mixture of synovial fluid with EDTA in the tube (inversion of the EDTA tube multiple times immediately after filling)
Viscosity (treatment with hyaluronidase required)
Pus, fibrinogen resulting in clots (counting in a conventional haemocytometer chamber).
Clots during transport to the laboratory or while awaiting testing
Lysis of cells during transport to the laboratory or while awaiting testing.

The list in this table is not exhaustive.

Table 2. Selected publications revealing cut-off values for synovial cell count and differential in patients with periprosthetic hip and knee joint infections.

References	Sample number	Joint	Cut-off Leukocytes	Cut-off % PMN
[4]	133 patients	Knee	>1700 cells/μL	>65%
[10]	429 joints	Knee	>1100 cells/μL	>64%
[7]	150 cases in 145 joints and 144 patients	Knee	≥3000 cells/μL	>75%
[6]	803 patients† 871 joints	Knee + Hip	>3450 cells/μL[a] >3444 cells/μL[b]	>78%[a] >75%[b]
[9]	75 patients	Knee + Hip	>1590 cells/μl	>65%
[1]	202 joints 178 patients	Hip	(>50.0 x 10^9 cells/L) >50000 cells/μL&	>80%
[5]	235 joints 220 patients	Hip	>4200 cells/μL >3000 cells/μL*	>80%
[8]	453 patients‡	Hip	3966 cells/μL	>80%

Footnotes:

*When synovial cell count results was combined with an elevated erythrocyte sedimentation rate and C-reactive protein level, the optimal cut-off value was >3000 cells/μL.

†Study including 810 patients with noninflammatory[a] and 61 patients with inflammatory arthritis[b].

‡ The study focusses on chronic PJI.

& Cut-off defined prior to the study without ROC curve.

Competing Interests

The authors have declared that no competing interest exists.

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